Ovarian ageing: the role of mitochondria in oocytes and follicles

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Résumé en anglais	BACKGROUND: There is a great inter-individual variability of ovarian ageing, and almost 20% of patients consulting for infertility show signs of premature ovarian ageing. This feature, taken together with delayed childbearing in modern society, leads to the emergence of age-related ovarian dysfunction concomitantly with the desire for pregnancy. Assisted reproductive technology is frequently inefficacious in cases of ovarian ageing, thus raising the economic, medical and societal costs of the procedures. OBJECTIVE AND RATIONAL: Ovarian ageing is characterized by quantitative and qualitative alteration of the ovarian oocyte reserve. Mitochondria play a central role in follicular atresia and could be the main target of the ooplasmic factors determining oocyte quality adversely affected by ageing. Indeed, the oocyte is the richest cell of the body in mitochondria and depends largely on these organelles to acquire competence for fertilization and early embryonic development. Moreover, the oocyte ensures the uniparental transmission and stability of the mitochondrial genome across the generations. This review focuses on the role played by mitochondria in ovarian ageing and on the possible consequences over the generations. SEARCH METHODS: PubMed was used to search the MEDLINE database for peer-reviewed original articles and reviews concerning mitochondria and ovarian ageing, in animal and human species. Searches were performed using keywords belonging to three groups: 'mitochondria' or 'mitochondrial DNA'; 'ovarian reserve', 'oocyte', 'ovary' or 'cumulus cells'; and 'ageing' or 'ovarian ageing'. These keywords were combined with other search phrases relevant to the topic. References from these articles were used to obtain additional articles. OUTCOMES: There is a close relationship, in mammalian models and humans, between mitochondria and the decline of oocyte quality with ageing. Qualitatively, ageing-related mitochondrial (mt) DNA instability, which leads to the accumulation of mtDNA mutations in the oocyte, plays a key role in the deterioration of oocyte quality in terms of competence and of the risk of transmitting mitochondrial abnormalities to the offspring. In contrast, some mtDNA haplogroups are protective against the decline of ovarian reserve. Quantitatively, mitochondrial biogenesis is crucial during oogenesis for constituting a mitochondrial pool sufficiently large to allow normal early embryonic development and to avoid the untimely activation of mitochondrial biogenesis. Ovarian ageing also seriously affects the dynamic nature of mitochondrial biogenesis in the surrounding granulosa cells that may provide interesting alternative biomarkers of oocyte quality. WIDER IMPLICATIONS: A fuller understanding of the involvement of mitochondria in cases of infertility linked to ovarian ageing would contribute to a better management of the disorder in the future.
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